REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication January 24, 2006.

Status of the Claims

Claims 1-3 and 5-17 are examined and prior pending in the Application. Applicants have above cancelled claims 1-3 and 5-17 without prejudice and now present new claims 34-50, directed to the elected subject matter, which are provided as a clear set of claims to more particularly point out and distinctly claim an aspect of the invention and are presented new for ease of review and consideration by the Examiner. New claims 34-46 as presented are fully supported by the prior claims and generally throughout Applicant's Specification.

Maintained Rejections

The Specification Fully Enables the Claimed Invention

The Examiner has again rejected claims 1-3 and 5-17 under 35 U.S.C. 112, first paragraph, stating that the Specification, while being enabling for a method of treating cardiac disease in a mammal comprising administering an effective amount of a compound selected from a dominant negative Mst1 (K59R) and XIAP does not reasonably provide enablement for such method comprising administering a compound or agent that blocks or otherwise inhibits Mst1 or Mst1 pathway. Applicants respectfully disagree and assert that the instant invention first identifies and recognizes the role and importance of Mst1 and the use of Mst1 modulators in treating cardiac disease and in cardioprotection. It is well within the skill of the artisan to identify and use other Mst1 inhibitors, particularly in view of the teaching and description in the instant Specification. Without prejudice to further and future prosecution, Applicants have above provided a clean set of new claims for the Examiner's consideration. Applicants submit that the above presented method claims are fully enabled by the Specification.

In view of the foregoing remarks and amendments, Applicants submit that the Examiner's rejection under 35 U.S.C. 112, first paragraph may properly be withdrawn.

Claim Rejections – 35 U.S.C. §102

Claims 1-3, 5-6, 8-10 and 13-14 remain rejected under 35 U.S.C. 102(a) as being anticipated by Yamamoto et al., 2001, which the Examiner asserts, teaches that cardiac myocytes were transfused with adenoviral vector harboring XIAP (X-linked inhibitor of apoptosis protein) and that overexpression of XIAP abolished morphological changes, increases in DNA fragmentation, activation of caspase-3 and myocyte death caused by chelerythrine. Applicants again disagree and assert that Yamamoto et al. does not anticipate claims 1-3, 5-6, 8-10 and 13-14 as prior pending. Yamamoto does not teach or describe anything with regard particularly to Mst1 or Mst1 specific inhibitors. Anticipation is a question of fact. Further, Applicants assert that the above amendments and claims obviate this rejection.

The Examiner again rejects claims 1-3 and 5-15 under 35 U.S.C. 102(b) as anticipated by Han et al., U.S. Patent No. 6,225,288, which discloses pharmaceutical compositions comprising compounds of formula I useful as inhibitors of caspase-3, which is implicated in modulating apoptosis. Anticipation is a question of fact. Han does not teach or describe anything with regard particularly to Mst1 or Mst1 inhibitors. Applicants assert that the above amendments and claims obviate this rejection.

Claims 1-3, 7-9 and 13-14 are again rejected under 35 U.S.C. 102(e) as being anticipated by Laugwitz et al., U.S. Patent Publication No. 2003/0130216. Laugwitz et al. relates to the use of inhibitor of caspase-3 or caspase-activated deoxyribonuclease (CAD) for the prevention or treatment of cardiac disease, particularly insufficiency of the left ventricle. The Examiner argues that Laugwitz et al teach all the elements of claims 1-3, 7-9 and 13-14. Laugwitz does not teach or describe anything with regard particularly to Mst1 or Mst1 specific inhibitors. Anticipation is a question of fact. Applicants assert that the above amendments and claims obviate this rejection.

In view of the foregoing remarks and amendments, Applicants submit that the Examiner's rejections under 35 U.S.C. 102 may properly be withdrawn.

Claim Rejections – 35 U.S.C. §103

Claims 10-12 remain rejected under 35 U.S.C. 103(a) as unpatentable over Han et al., U.S. Patent No. 6,225,288, in view of Danilewicz et al., U.S. Patent No. 4,975,444. Danilewicz

et al. teach a series of cycloalkyl-substituted glutaramide derivatives which are antihypertensive agents having utility in treatment of cardiovascular disorders and able to inhibit angiotension converting enzyme. Danilewicz teaches that the compounds may be co-administered with other agents for treatment of cardiac conditions. The Examiner argues that it would have been obvious to the skilled artisan at the time the invention was made to combine Han et al. and Danilewicz et al. Applicants respectfully disagree. As noted above Han et al discloses pharmaceutical compositions comprising compounds of formula I useful as inhibitors of caspase-3, which is implicated in modulating apoptosis, but does not describe or teach anything with regard particularly to Mst1 or Mst1 specific inhibitors. The combination of Han and Danilewicz does not teach or suggest the use or combination of specific Mst1 inhibitors with any other compounds for treatment of cardiac disease. In particular and in view of the above claim amendments and presented claims, the combination of Han and Danilewicz does not make obvious the claimed invention.

Claims 15-17 are again rejected under 35 U.S.C. 103(a) as unpatentable over Han et al., U.S. Patent No. 6,225,288 in view of Kukreja, U.S. Patent Publication No. 2004/0009957. Kukreja teaches exposing cells, tissues, organs to a phosphodiesterase-5 (PDE-5) inhibitor to prevent or decrease apoptosis or necrosis prior to, after or during an ischemia/reperfusion event. Further, Kukreja teaches administration of PDE-5 inhibitors to patients undergoing treatment with Doxorubicin to prevent or lessen Doxorubicin-induced cardiotoxicity. The Examiner asserts it would have been obvious to co-administer an inhibitor of Mst1 with Doxorubicin to reduce Doxorubicin-induced cardiotoxicity as taught by Han et al. and Kukreja et al. Applicants disagree. As noted above Han et al discloses pharmaceutical compositions comprising compounds useful as inhibitors of caspase-3, which is implicated in modulating apoptosis, but does not describe or teach anything with regard particularly to Mst1 or Mst1 specific inhibitors. The combination of Han and Kukreja does not teach or suggest the use or combination of specific Mst1 inhibitors with any other compounds for treatment of cardiac disease. In particular and in view of the above amendments and presented claims, the combination of Han and Kukreja does not make obvious the claimed invention.

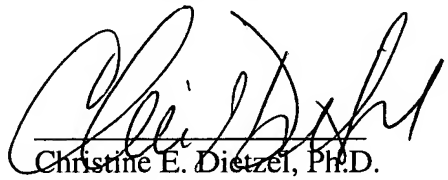
In view of the foregoing remarks and amendments, Applicants submit that the Examiner's rejections under 35 U.S.C. 103 may properly be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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